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10/599,203	09/22/2006	Yoshinobu Yamazaki	Q96974	5777

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EXAMINER	
PAGONAKIS, ANNA	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,203	YAMAZAKI ET AL.	
	Examiner	Art Unit	
	ANNA PAGONAKIS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/16/2008 & 1/26/2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *1-10,15,16 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-14 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 sheet, 2/6/2008; 4 sheets, 9/22/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of silodosin and ethyl(-)-2-[4-[2-[[(1S,2R)-2-hydroxy-2-(4-hydroxyphenyl)-1-ethylethyl]amino]ethyl]-2,5-dimethylphenoxy]acetate in the reply filed on 10/16/2008 is acknowledged. The structural compound of silodosin was submitted by Applicant on 1/26/2009. The traversal is on the ground(s) that special technical feature is "rather straight forward" and that the special technical features of the groups have been misunderstood. This is not found persuasive because Applicant has simply allege that the special technical feature is "rather straight forward" and that the special technical features of the groups have been misunderstood and provide no basis or evidence in support of their allegation. The traversal is that the argued special technical feature contained in general formula I of phenooxacetic acid derivatives are known to the art. Silodosin and the phenoxyacetic acid are known to the art therefore the compositions and methods lack unity of invention because the technical feature linking the groups is not "special" within the meaning of PCT Rule 13.1.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-18 are pending in the application. Claims 1-10, 15-16 and 18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Accordingly, claims 12-18 are newly added and no claims have been amended or cancelled.

This application is the national stage entry of PCT/JP2005/004825 filed 3/17/2005; and claims benefit of foreign priority document JAPAN PCT/JP2004/004000 filed 3/24/2004; currently an English translation of this foreign priority document has not been filed.

Claims 11-14 and 17 are currently under examination and the subject of this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-14 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification while enabling for treating urinary incontinence with a phenoxyacetic acid derivative and silodosin, does not reasonably provide enablement for preventing urinary incontinence with a phenoxyacetic acid derivative and silodosin or does not reasonably provide enablement for a method for the treatment of urinary frequency or incontinence, comprising administering… a *hydrate or solvate* of the phenoxyacetic derivative of the formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per factors indicated in the decision In re Wands, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation.

The factors include:

1. the quantity of experimentation necessary
2. the amount of direction or guidance provided
3. the presence or absence of working examples
4. the nature of the invention
5. the state of the art
6. the relative skill of those in the art
7. the unpredictability of the art and
8. the breadth of the claims

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice that instant invention without resorting to undue experimentation in view of the further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to a method for preventing urinary incontinence with a phenoxyacetic acid derivative and silodosin.

The relative skill of those in the art is generally that of an Ph.D. or M.D.

There are no known preventive therapies for urinary incontinence in the art.

It is clear the art to which the present invention relates is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical efficacy.

The breadth of the claims

The claims are very broad and inclusive of any "causes" of urinary incontinence.

The amount of direction or guidance provided and the presence or absence of working examples

There are no examples showing the instant a method for preventing urinary incontinence with a phenoxyacetic acid derivative and silodosin. No examples showing phenoxyacetic acid derivative and silodosin is administered to a healthy subject not having urinary incontinence, and the administration of the instant phenoxyacetic acid derivative and silodosin will prevent the subject from having urinary incontinence during its lifetime. Current modes of treatment are known, but there are no known agents, which can be, prevent the causes of urinary incontinence in a healthy subject.

The working examples only show the elected phenoxyacetic acid, ethyl(-)-2-[4-[2-[[(1S,2R)-2-hydroxy-2-(4-hydroxyphenyl)-1-ethylethyl]amino]ethyl]-2,5-dimethylphenoxy]acetate, to treat urinary incontinence in a patient.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to which cause would be prevented for urinary incontinence. The skilled artisan would expect the interaction of a particular drug in the prevention of causes of urinary incontinence to be very specific and highly unpredictable absent a clear understanding

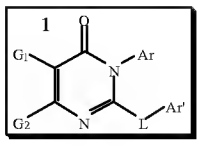
of the structural and biochemical basis of the agent. The instant specification sets forth no such understanding nor any criteria for extrapolating beyond the administration of the ethyl(-)-2-[4-[2-[[(1S,2R)-2-hydroxy-2-(4-hydroxyphenyl)-1-ethylethyl]amino]ethyl]-2,5-dimethylphenoxy]acetate. Even for the data presented, no direction is provided to prevent specific causes of urinary incontinence. Absent reasonable *a priori* expectations of success, one skilled in the art would have to test extensively many conditions that may lead to urinary incontinence to discover which cause is prevented. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do so otherwise.

Solvates and hydrates of formula I

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is *undue*. These factors include, but are not limited to: (a) breadth of the claims; (b) nature of the invention; (c) state of the prior art; (d) level of one of ordinary skill in the art; (e) level of predictability in the art; (f) amount of direction provided by the inventor; (g) existence of working examples; and (h) quantity of experimentation needed to make or use the invention based on the content of the disclosure. (See *Ex parte Forman* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

The above factors, regarding the present invention, are summarized as follows:

(a) *Breadth of the claims* - the breadth of the claims includes a method for the treatment of urinary frequency or incontinence by administering a phenoxyacetic derivative and an alpha1 adrenoreceptor blocker, comprising administering… a phenoxyacetic derivative of the formula I;



(b) *Nature of the invention* - the nature of the invention is a method method for the treatment of urinary frequency or incontinence by administering a phenoxyacetic derivative and an alpha1 adrenoreceptor blocker, comprising administering… a phenoxyacetic derivative or pharmaceutical preparation of the formula I or a salt thereof;

(c) *State of the prior art* - *Nature Reviews: Drug Discovery* offers a snapshot of the state of the drug development art. Herein, drug development is stated to follow the widely accepted Ehrlich model which includes: 1) development of a broad synthetic organic chemistry program; 2) subsequent testing of compounds in an appropriate laboratory model for the disease to be treated; and 3) screening of compounds with low toxicity in prospective clinical trials (Jordan, V. C. *Nature Reviews: Drug Discovery*, 2, **2003**, p. 205);

(d) *Level of one of ordinary skill in the art* - the artisans synthesizing applicant's *solvate(s) or hydrate(s)* of a substituted quinazolinone or pharmaceutical preparation of the formula I or a salt thereof, would be a collaborative team of synthetic chemists and/or health practitioners, possessing commensurate degree level and/or skill in the art, as well as several years of professional experience;

(e) *Level of predictability in the art* - Synthetic organic chemistry is quite unpredictable (*In re Marzocchi and Horton* 169 USPQ at 367 ¶ 3). The following excerpt is taken from Dörwald, which has extreme relevance to the synthesis of *oxidative metabolite(s)* of substituted quinazolinones or pharmaceutical preparations of the formula I or salts thereof (Dörwald, F. Zaragoza. *Side Reactions in Organic Synthesis: A Guide to Successful Synthesis Design*, Weinheim: WILEY-VCH Verlag GmbH & Co. KGaA, **2005**, Preface):

Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why.

Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work.

Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious).

Similarly, the following excerpt is taken from Vippagunta, et al. with respect to the synthesis of *solvates* and *hydrates* of substituted quinazolinones or pharmaceutical preparations of the formula I or salts thereof (Vippagunta, et al. *Advanced Drug Delivery Reviews*, 48, **2001**, p. 18):

Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds. Certain molecular shapes and features favor the formation of crystals without solvent; these

compounds tend to be stabilized by efficient packing of molecules in the crystal lattice, whereas other crystal forms are more stable in the presence of water and/or solvents. There may be too many possibilities so that no computer programs are currently available for predicting the crystal structures of hydrates and solvates.

Finally, the following excerpt is taken from Burger's with respect to the synthesis of *prodrugs* of substituted quinazolinones or pharmaceutical preparations of the formula I or salts thereof (Wolff, Manfred E., Ed. *Burger's Medicinal Chemistry and Drug Discovery - Fifth Edition,* New York: John Wiley & Sons, **1996**, vol. 1, pp. 975-976):

The design of prodrugs in a rational manner requires that the underlying causes which necessitate or stimulate the use of the prodrug approach be defined and clearly understood. It may then be possible to identify the means by which the difficulties can be overcome. The rational design of the prodrug can thus be divided into three basic steps: (1) identification of the drug delivery problem; (2) identification of the physiochemical properties required for optimal delivery; and (3) selection of a prodrug derivative that has the proper physiochemical properties and that will be cleaved in the desired biological compartment.

The difficulty of extrapolating data from animal to humans encountered during toxicokinetic and toxicologic studies with drugs is amplified with prodrugs, since not only metabolism of the active moiety might differ, but also its availability from the prodrug. As a matter of fact, there is presently no published rational for the conduct of animal and human pharmacokinetic programs during prodrug research and development.

(f) *Amount of direction provided by the inventor* - the application is negligent regarding direction with respect to making and using (performing) a method for the treatment of urinary frequency or incontinence by administering a phenoxyacetic derivative and an alpha1 adrenoreceptor blocker, comprising administering… a *solvate or hydrate* of a phenoxyacetic acid for formula I;

(g) *Existence of working examples* - applicant has provided sufficient guidance to make and use (perform) a method for the treatment of urinary frequency or incontinence by administering a phenoxyacetic derivative and an alpha1 adrenoreceptor blocker, comprising administering… a phenoxyacetic acid derivative of the formula I or a salt thereof; however, the disclosure is insufficient to allow extrapolation of the limited examples to enable the scope of performing a method for method for the treatment of urinary frequency or incontinence by administering a phenoxyacetic derivative and an alpha1 adrenoreceptor blocker, comprising administering… a *solvate or hydrate* of a phenoxyacetic derivative of the formula I. The specification lacks working examples of a method for method for the treatment of urinary frequency or incontinence by administering a phenoxyacetic derivative and an alpha1 adrenoreceptor blocker, comprising administering… a *solvate or hydrate* of a phenoxyacetic derivative of the formula I.

Within the specification, "specific operative embodiments or examples of the invention must be set forth. Examples and description should be of sufficient scope as to justify the scope of the claims. *Markush* claims must be provided with support in the disclosure for each member of the *Markush* group. Where the constitution and formula of a chemical compound is stated only as a probability or speculation, the disclosure is not sufficient to support claims identifying the compound by such composition or formula." See MPEP § 608.01(p).

(h) *Quantity of experimentation needed to make or use the invention based on the content of the disclosure* - predicting whether a recited compound is in fact one that produces a desired physiological effect at a therapeutic concentration and with useful kinetics, is filled with experimental uncertainty, and without proper guidance, would involve a substantial amount of experimentation (Jordan, V. C. *Nature Reviews: Drug Discovery,* 2, **2003**, pp. 205-213).

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. {*In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)}.

The determination that *undue experimentation* would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. (*In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404). These factual considerations are discussed comprehensively in MPEP § 2164.08 (scope or breadth of the claims), § 2164.05(a) (nature of the invention and state of the prior art), § 2164.05(b) (level of one of ordinary skill), § 2164.03 (level of predictability in the art and amount of direction provided by the inventor), § 2164.02 (the existence of working examples) and § 2164.06 (quantity of experimentation needed to make or use the invention based on the content of the disclosure).

Based on a preponderance of the evidence presented herein, the conclusion that applicant is insufficiently enabled for making and using (performing) a method for the treatment of urinary frequency or incontinence by administering a phenoxyacetic derivative and an alpha1 adrenoreceptor blocker, comprising administering… a *solvate or hydrate* of a phenoxyacetic derivative of the formula I, is clearly justified.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-14 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "characterized" in claim 11 is a relative term which renders the claim indefinite. The term is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree and one of ordinary skill in the art would not reasonably be appraised of the scope of the invention. It is suggested that Applicants use conventional transitional phrases for US patent prosecution practice. Amendment to the claims to replace "characterized by" to –comprising- would obviate this issue.

LACK OF WRITTEN DESCRIPTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

Claims 11-14 and 17 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses chemicals, such as hydrates or solvateswhich meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claims 11-14 and 17 is(are) directed to encompass hydrates and solvates, which only correspond in some undefined way to specifically instantly disclosed chemicals. None of these hydrates or solvates meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. The specification

provides insufficient written description to support the genus encompassed by the claim, and one of skill in the art would recognize that Applicants were not in possession of the claimed invention because the art is replete with difficulties of synthesis and efficacy as set forth below. For example, synthetic organic chemistry is known by the skilled artisan to be quite unpredictable as evidenced by Dorwald (Dorwald, F. Zaragora, Side Reactions in Organic Synthesis: A guide to Successful Synthesis, Weinheim: WILEY-VCH Verlag GmbH & Co. KGaA, 2005, Preface): "Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why.

Despite the many pitfalls in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise demanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work.

Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed derivatives, analogs, etc., regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only the above chemically structurally defined chemicals, but not the full breadth of the claim(s) meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See page 1115.)

Claim Rejections - 35 USC § 103

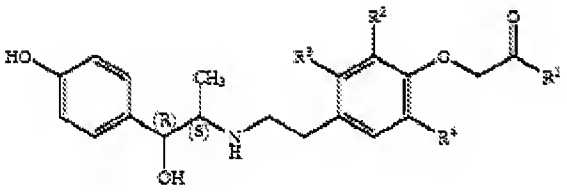
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11-14 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanaka et al (WO 00/02846, cited as a functional language equivalent is U.S. 6,538,152) and Ford (Drug Discovery World, Fall 2003).

Tanaka et al teach the administration of the compound:



where R2 and R3 are ach lower alkyl groups and pharmaceutically acceptable salts thereof, for the treatment of urinary incontinence (abstract).

Ford teaches the use of silodosin for the treatment of urinary incontinence (Table 2B).

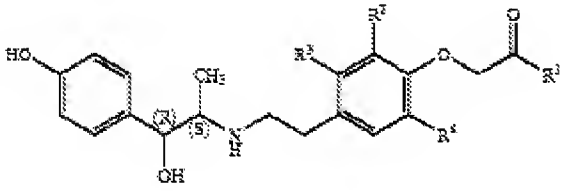
Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to administer silodosin (alpha-adrenoreceptor antagonist) in combination with ethyl(-)-2-[4-[2-[[(1S,2R)-2-hydroxy-2-(4-hydroxyphenyl)-1-ethylethyl]amino]ethyl]-2,5-dimethylphenoxy]acetate in view of teachings of Tanaka et al and Ford et al. One would have been motivated to do so because each of the therapeutics have been individually taught in the prior art to be useful for the treatment of urinary incontinence. Therefore, the idea of combining administration of the two agents flows logically from their having been individually

taught in the prior art. Applying the same logic to the instant claims, one of ordinary skill in the art would have been imbued with a reasonable expectation of success that administration of both agents would be useful for the treatment of urinary incontinence.

With respect to claim 17, the determination of a dosage having the optimum therapeutic index while minimizing adverse and/or unwanted side effects is well within the level of the skilled artisan. The dosage is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would have been obvious for a person of ordinary skill to determine the optimal dosage needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of dosages would have been obvious at the time of Applicant's invention.

Claims 11-14 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanaka et al (WO 00/02846, cited as a functional language equivalent is U.S. 6,538,152) in view of Broten et al (U.S. 6.410.554) in light of the Mesh Supplementary Data (2009).

Tanaka et al teach the administration of the compound:



where R2 and R3 are ach lower alkyl groups and pharmaceutically acceptable salts thereof, for the treatment of urinary incontinence (abstract).

Broten et al teach administration of KMD-3213 for the treatment of lower urinary tract symptoms which including increasing urine flow rate, decreasing residual urine volume and improving overall obstructive and irritative symptoms in patients with benign prostatic hyperplasia or symptomatic

prostatism (column 5). KMD-3213 can be administered at a dosage from about 0.01 mg to about 500 mg per subject (column 13).

Mesh Supplementary data teaches that KMD-3213 is an alternative name for silodosin.

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to administer silodosin (alpha-adrenoreceptor antagonist) in combination with ethyl(-)-2-[4-[2-[[(1S,2R)-2-hydroxy-2-(4-hydroxyphenyl)-1-ethylethyl]amino]ethyl]-2,5-dimethylphenoxy]acetate in view of teachings of Tanaka et al and Broten et al. One would have been motivated to do so because each of the therapeutics have been individually taught in the prior art to be useful for the treatment of urinary incontinence. Therefore, the idea of combining administration of the two agents flows logically from their having been individually taught in the prior art. Applying the same logic to the instant claims, one of ordinary skill in the art would have been imbued with a reasonable expectation of success that administration of both agents would be useful for the treatment of urinary incontinence.

With respect to claim 17, the determination of a dosage having the optimum therapeutic index while minimizing adverse and/or unwanted side effects is well within the level of the skilled artisan. The dosage is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would have been obvious for a person of ordinary skill to determine the optimal dosage needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of dosages would have been obvious at the time of Applicant's invention.

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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AP

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